Platelet-Rich Plasma Injection Efficacy in Tendinopathy in Adult Patients: A Critically Appraised Topic

An Honors Thesis (HONR 499)

by

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Abstract

Tendinopathy is any injury to a tendon. With an injury to the tendon sheath or tendon, the injury response phase is activated, which is mediated by growth factors. A growth factor is a physiological component of plasma in the blood. These factors bind and signal for proteins to regulate cellular processes to aid in the healing of tissue. With this understanding of how growth factors in blood platelets aid in the healing process, a platelet-rich plasma (PRP) injection has been developed. In a PRP injection, the increase in platelet concentration is thought to promote cell proliferation in patients suffering from chronic tendon pathologies. After developing a clinical question, I attempt to answer it by analyzing four recent studies.

Acknowledgments

I would like to thank Dr. Dorice Hankemeier for advising me through this project, as well as my past four years in the athletic training program.

I would like to thank Dr. Scott Taylor for inspiring me to pursue this compilation of research in an area that has not been fully looked into.

I would like to thank Dr. Jennifer Popp and Dr. Stacy Walker. Their guidance and help the last four years does not go unnoticed.

Process Analysis

Over the course of being in the Athletic Training program, I have been exposed to many different treatment options for patients suffering from chronic pathologies. During my senior fall semester, I had the opportunity to learn from a physiatrist. After talking to him about new and upcoming topics in the medical world, he suggested I look into platelet-rich plasma injections (PRP). The PRP injection uses a person's body to attempt to heal their body. I thought that this was a very unique and interesting concept that inspired me to write a critically appraised topic focusing on the effects of PRP injections on patients with tendinopathy. As many athletes deal with tendinopathy at some point and time during their athletic career, I wanted the research to support PRP injections as a treatment modality for these people chronically suffering.

Once my topic was established, the first step to finding information was using the library databases as outlined in my thesis to gather the necessary data. Once I found four articles related to my clinical question I was able to analyze this to form an opinion and conclusion. To share the research and conclusions I found during my research, I have written a critically appraised topic for medical colleagues to be able to reference multiple opinions in one place. I also created a poster that was presented to my peers and advisors during the program end of the year banquet. In addition to this brief presentation, I also presented in a formal setting to my peers and advisors. Throughout this experience I have learned the value of continuing education as I enter into a professional career as an athletic trainer. I will continue to seek new learning opportunities in order to provide the best patient centered care as a health care provider.

Clinical Scenario

Tendinopathy is any injury to a tendon that can range from an acute injury such as a tear to a chronic tenosynovitis. Specifically, tenosynovitis is a degeneration of the tendon, which results in the inflammation of the tendon sheath. With an injury to the tendon sheath or to the tendon, the injury response phases are activated. During the first phases of injury response, healing commences and is mediated by growth factors. More specifically, growth factors bind to cell-surface receptors and initiate an intracellular signal resulting in protein formation[1]. The newly formed proteins regulate cell proliferation, cellular chemical movement, new blood cell formation, cell differentiation, and extracellular matrix formation; indicative of regeneration and healing[1]. Platelets in a patient's blood are known to contain many of these desirable growth factors[1]. The healing of tendons occurs through a dynamic process in 3 overlapping growth factor regulated phases. In a platelet-rich plasma injection, these growth factors are increased in concentration. In vitro, the platelet rich plasma (PRP) injection has been shown to promote cell proliferation, indicating the ability to halt excess inflammation while activating proliferation and maturation[2]. In recent studies, research suggests that the growth factors in platelet-rich plasma (PRP) will expedite the healing process and in turn decrease the perception of pain and improve function of an affected joint.

Focused Clinical Question

Do platelet-rich plasma injections improve perceived pain and function of adult patients with tendinopathy in the body?

Summary of Search, "Best Evidence" Appraised, and Key Findings

- The literature was search for studies of level 3 or higher that investigated the effects of PRP injections on pain and function in patients with diagnosed tendinopathy.
- The literature search identified seven possible studies related to the clinical question; three randomized control trials[3,4,5] and 1 cohort study[6] met the inclusion criteria set for this critically appraised topic.
- Of the included articles, three studies[3,4,5] examined the effects of platelet-rich plasma injections compared to a control. One study[6] looked at the effects of one PRP injection in patients with tendinopathy over time. All studies included measures of pain as well as function through the use of a patient related outcome measure (PROM) each varying based on injury location.
- Overall, three studies[3, 4, 5] concluded PRP injections were a not better than placebo treatment option for patients with tendinopathy, while one studies[6] indicated there was statically significant difference in PRP injection versus no treatment.

Clinical Bottom Line

There is inconsistent evidence to support the use of PRP injections on perception of pain and function in individuals with tendinitis or tendinopathy. Pain did decrease in patients however not significantly when compared to a placebo group. Function did not improve faster compared with a saline or autologous blood injections. PRP injections did show a decrease in pain and an increase in function however; PRP injections did not show any difference in improvements from placebo treatments or naturally healing body.

Strength of Recommendation

There is a grade "B" evidence to support the use of PRP injection to decrease pain and increase function in patients with tendinopathy as determined by the inconsistency of studies[3-6].

Search Strategy

Terms Used to Guide Research Strategy

- **P**atient/Client group: patients with tenosynovitis
- **I**ntervention: platelet-rich plasma injection
- **C**omparison: None
- **O**utcomes: perceived pain and function

Sources of Evidence Searched

- CINAHL
- PubMed
- Sports Discus
- MedLine

Inclusion and Exclusion Criteria

Inclusion Criteria

- English Language
- Published in last 10 years
- Level of evidence of 3 or higher
- Participants age 18 years or older
- Human beings
- Patients treated with PRP injection
- Patients with tendinopathy

Exclusion Criteria

- Not available in English
- Published prior to 2007
- Case Study, Case Series, or lower than level of evidence of 3
- Patients without tenosynovitis
- Patients younger than 18 years of age

Results of Search

Level of Evidence	Study Design	Reference
2	RCT	Creaney et al[3], Kesikburun et al[4], Krogh et al[5]
3	Cohort	Sanli et al[6]

Table 1: Summary of Study Designs of Articles Retrieved

Four studies were located and categorized as shown in Table 1 (based on levels of evidence, Centre for Evidence Based Medicine, 2011)[7].

Best Evidence

The following studies (Table 2) were identified as the best evidence and selected for inclusion in this critically appraised topic (CAT). Reasons for selecting these studies were they were a level of evidence of 3 or higher, included patients diagnosed with tendinopathy, and examined the effectiveness of platelet-rich plasma injections as a modality to treat pain and improve function.

Implications for Practice, Education, and Future Research

A platelet-rich plasma injection contains bioactive elements for musculoskeletal tissue healing and has been an interest of orthopedic surgeons for many years. In normal blood, the platelet count ranges from 150,000/μL to 350,000/μL[1]. Platelets are cytoplasmic fragments of megakaryocytes and play a role in cellular hemostasis[1]. Platelets are known to release a burst of proteins that contribute to the healing processes commonly referred to as growth factors, which create tissue specific responses. By increasing the concentration of platelets to one million per microliter, the amount of growth factor present is increased by three to five-fold[2]. The growth factors bind to the transmembrane receptors in the cell, initiate a signal within the cell, and ultimately result in new protein formation, which is responsible for cell proliferation, cellular chemotaxis, angiogenesis, cell differentiation, and

	Creaney et al[3]	Kesikburun et al[4]	Krogh et al[5]	Sanli et al[6]
Study Design	Randomized Control Trial	Randomized Control Trial	Randomized Control Trial	Cohort
Participants	150 participants (85 male, 65 female) with a mean age of 50 years who had failed previous conservative therapy including physical therapy exercises (stretches and eccentric loading) for elbow tendinopathy and had symptoms for a minimum of 6 months. Exclusion criteria included patients who previously had corticosteroid, dry-needling, or a blood injection.. 80 participants were assigned to the PRP injection group, while 70 participants were assigned to the blood control group. Patients were blinded to which group they were randomly assigned. 87% of the participants were analyzed at follow-up date.	40 patients (18-70 years of age) with a history of shoulder pain for longer than 3 months during overhead activities, MRI findings indicating rotator cuff tendinopathy (RCT) or partial tendon ruptures, and a minimum of 50% reduction in shoulder pain with subacromial injections of an anesthetic. Patients were randomly and blindly assigned to a PRP group (n=20) and a placebo group (n=20). Exclusion criteria included a full thickness tear, presence of another disease that may cause shoulder pain, a systemic disease, a hemoglobin level lower than 11g/dL, pregnancy, or a history of subacromial or intra-articular steroid injection. 97.5% of the participants were available for final follow-up assessment.	24 patients with Achilles tendinopathy (AT) were included. The patients must have had AT symptoms for more than 6 months, a clinical diagnosis with pain and thickened tendon, and an ultrasound diagnosis of thickened tendon and visual signs of tendinopathy. Exclusion criteria included patients younger than 18 years of age, glucocorticoid injection, previous AT surgery, or any known inflammatory disease. The groups were randomly allocated, 12 in each group. There was no dropout at the 3 month time period. However 16 patients dropped out prior to the 12-month assessment due to unsatisfactory effects. Six patients remained in the placebo group, while two remained in the PRP group for the 12-month follow up exam. 33% of the participants were available for the final follow-up assessment.	12 participants (10 male, 2 female) were included in this study. The median age was 41 years. The participants were eligible if they were 18 years or older, unresponsive to physical therapy, non-steroidal anti-inflammatory, or steroid injections, and had a diagnosis of distal biceps tendonitis. Exclusion criteria were pregnancy, systemic diseases, previous surgery for elbow tendinitis, neurological disorders, uncooperative patients, steroid injection within 3 months or complete tendon rupture. 100% were present for follow up.
Intervention Investigated	Patients in both groups were injected first with 2ml bupivacaine, followed by a 2-minute wait. Then patients were injected with 1.5mL blood (234 platelets X 10^9/injection) or 1.5mL PRP (652 platelets X 10^9/injection) to the affected elbow according to grouping. Patients were then instructed to continue normal activities while avoiding physical activity or heavy lifting. Ice was allowed as well as analgesic. Patients were instructed to avoid NSAIDs. The same blinded operator using same technique for all patients performed injections. All patients had two injections at time 0 and 1 month.	All participants, clinician and evaluator remain blinded throughout the study. In all participants, injections were made under the posterolateral aspect of the acromion using real-time ultrasound guidance. First a 1% lidocaine injection was administered followed by the designated solution, 5mL PRP with a four fold increase in platelets or 5mL saline solution. After the injection, patients remained lying supine without moving the shoulder for 15 minutes. All patients then underwent a standard rehabilitation protocol for a total of 6 weeks and were told to rest from all overhead activity in the first 2 days.	All patients underwent an ultrasound-guided injection technique. PRP and saline were injected into 7 tendon perforations in the thickest part of the tendon. 6mL of saline was injected for the control group. In the PRP injection, 6mL of PRP with a platelet concentration increased on average by 8 fold compared with whole blood. Patients were advised to minimize strain on AT and gradually increase rehabilitation below pain limit. The rehabilitation was an at-home standard protocol, however the length of this protocol was not stated. This study was single blinded.	All patients had an ultrasound-guided injection performed in a supine position by two clinicians. The injection of three microliters of L-PRP and sodium bicarbonate buffer was administered to the distal end of the biceps tendon. Post treatment regime included eccentric exercises to biceps and tendon.

Table 2: Characteristics of Included Studies

	Creaney et al[3]	Kesikburun et al[4]	Krogh et al[5]	Sanli et al[6]
Outcome Measures	Patient-Related tennis elbow evaluation (PRTEE) score was used to measure pain and physical function. The range of scores for the PRTEE is 0-100. PRTEE was completed at baseline, 1 month, 3 months, and 6 months. The same assistant administered the questionnaire each time.	The primary outcome measure was the Western Ontario Rotator Cuff (WORC) Index, which assesses the quality of life for patients suffering from rotator cuff disease. The score possible ranged from 0-2100, the higher score indicating worse functioning. The secondary outcome measures were the Shoulder Pain and Disability Index (SPADI) scores represented as a percentage 0-100%, the Neer impingement sign (using VAS score for pain 0-10), and a passive range of motion test using a goniometry. Outcome measures were assessed at baseline, 3 weeks, 6 weeks, 12 weeks, 24 weeks, and 1 year after the injection by a blinded researcher.	The primary outcome measure was the VISA-A after 3 months. The VISA-A is a Danish patient related outcome measure. The secondary outcome measures were changes in pain at rest, when walking, and when AT was squeezed. The VISA-A scores range from 0 to 100, 100 indicating optimal function. The pain scale used was 0, no pain, to 10, worst pain imaginable. The 3-month data was chosen as the primary data due to the extensive dropout rate.	The primary outcome measure was a Visual Analogue Scale (VAS) rest and activity pain scores on a scale of 0-10. The secondary outcome measure was the elbow functional assessment (EFA) score. The range of scores possible was 0-100. Outcome measures were assessed at baseline as well as at an average of 47 months post injection.
Main Findings	Over the course of 6 months, PRTEE scores decreased in both groups, indicative of decreased pain in both PRP injection patients as well as blood injection patients. 25 points on the scale showed clinically significant improvement. The mean score was a 49 at the beginning of the study. At baseline the PRTEE1 the mean was 45.8 for plasma and 52.5 in the blood group, indicating both groups are comparable. The mean score of PRTEE was 35.8 (95% CI 30.3 to 41.4) in the PRP injection group, where the mean PRTEE score was 46.8 (95% CI 42.1 to 51.5) in the blood injection group using a X^2 test. Both improvements were greater than the predetermined clinically significant improvement of 25. No statistical p values were reported.	In both treatment groups, significant improvement was seen in the WORC score at all assessment points (P<.001). The SPADI and VAS (Neer impingement sign) scores also showed similar improvement in both groups (P<.001). There was no statistical difference in the amount of improvement in scores between groups for any outcome measure at any time point (P>.063-.947).	There was no statistically significant difference between PRP and saline injections in the VISA-A (95% CI, P=.868). In the secondary outcome measures there were no statistically significant difference between groups. Pain at rest, P=.137, pain when walking P=.544, and pain when AT squeezed P= .208. Tendon thickness was the only place where there was a statically significant difference, P=.030, indicating an increase in tendon thickness after PRP injection.	All patients showed significant improvement in pain and function. The VAS pre-intervention score at rest was 6 and post intervention was 0.5 with p<.002. The VAS pre-intervention score during activity was 8 and post intervention was 2.5 with p<.002. The EFA pre-intervention score was 63 and post intervention score was 90 with p<.004. All patients were satisfied with outcomes at final follow-up.
Level of Evidence	1	1	1	3
Validity Score	PEDro 10/10	PEDro 10/10	PEDro 6/10	STROBE 19/22
Conclusion	PRP and blood injections are important as a secondary option for patients with elbow tendinopathy in which conservative treatment has failed. The primary treatment of elbow tendinopathy should remain conservative treatment.	PRP injections were found to be no more effective in improving quality of life, pain, disability, and shoulder range of motion than the placebo in patients with chronic rotator cuff disease within a 1-year study. PRP injections are not supported.	1 injection of PRP when compared with one injection of saline did not result in significant improvement in perceived quality of life or decrease pain with Achilles tendinopathy.	All patients showed a significant improvement in VAS rest and activity scores and improvement in EFA scores. US-guided PRP injections were an effective treatment for symptomatic distal biceps tendinopathy.

Table 2: Characteristics of Included Studies

extracellular matrix production[1]. The PRP injection is thought to increase the concentration of growth factors and will cause an increase in the recovery process[2].

The four studies[3-6] included in this CAT examined the relationship between platelet-rich plasma injections and perceived pain and function in individuals suffering from tendinopathy. The studies[3-5] divided individuals with tendinopathy into two groups that were associated with a PRP injection and a blood control group[3] and a PRP injection group and a saline control group[4-5]. The final study was a cohort study with PRP injection group[6]. Three of the studies[3-5] revealed there was no benefit of PRP injections versus an autologous blood injection or saline injection. Sanli et al[6] concluded there was a decrease in pain and an increase in function of a person with distal biceps tendinitis following PRP injection. Because there was no control or comparison, it is difficult to know how effective the treatment was on patients.

To create these PRP injections, the blood is typically collected through the antecubital vein. A centrifuge is then used to separate the platelets from the plasma. All studies included in this paper used different techniques to isolate the platelets. Because the platelets are collected from the individual patient, the concentration of platelets also varies. The differences in the PRP injections could have been a cause of the varying results from studies[3-6]. However, this variance in the injections is a naturally occurring error in the procedure and could not have been avoided in any of the studies.

The current applications of PRP injections indicate patients with tendonitis would benefit due to the increase in concentration of growth factors. However, this was not demonstrated in three out of the four studies. Wroblewski et al[2] stated PRP injections may halt the excess inflammation, which would inhibit the fibrous scar tissue that goes along

with the healing of tendon to bone. While the PRP injection does activate proliferation and maturation, the decreased inflammation associated with the altered healing process could suggest why three studies[3-5] showed no significant improvement compared to the control groups. The variation in the techniques of obtaining the platelet-rich plasma could have accounted for why no results were seen when compared to the control groups. Because different techniques were used a variation of concentrations of platelets was seen in all of the studies[3-5] with no report of concentration in the Sanli[6] study.

In addition to the differences in PRP injection, a variation in results could have been due to the focus solely on patient reported outcome measures. These measures take into account the minimal difference that is important to the patient, however this type of data can subjective person to person. Because of the strict focus on patient reported information, it makes it difficult to conclude that the PRP injection wasn't helping but instead to say that the thought of an injection in general was creating the necessary results for the patient to think they are benefitting. However typically when looking at medical related data, patient report data is of the highest value because of the focus on patient centered care. The outcome measures could be seen as a strength of the studies[3-6] or also as a deficit that could be overcome by objective data collection.

The study[5] by Krogh and his colleges was difficult to use because of the large number of dropouts that were reported. The large mortality rate caused the researchers to shift their data collection to the three-month post-injection exam rather than the twelve-month post-injection exam. No other study reported this high of a drop out rate. The participants in this study were allowed to drop out if they felt they were not achieving the results desirable and were able to switch to a different treatment plan. With this flexibility

in study design, it allowed a high percentage of drop out early in the study, which forced a change in data analysis. The subjects in this study were not obtaining the results they desired attributing to the conclusion of this study. The results of the study[5] did not support the use of PRP injections in the treatment of tendinopathy, similar to two of the other studies[3,4].

Biochemically, the PRP injection should help to decrease the symptoms of tendinopathy. However, it was not clinically proven to decrease pain or increase function any quicker than the normal healing process. More research in the future needs to be collected in a more athletic and younger population to be able to justify the use of the PRP injection with athletes for the treatment of tendinopathy or tendinitis. Because there were no adverse reactions to the PRP injection, it is a safe treatment option to try, which lends itself well to further research. In addition to a more specific patient population, the PRP injection could be looked at to treat an acute injury. By adding additional growth factors, it could add an additional kick-start to the healing process in the initial injury response process. More research needs to be completed to to definitively determine if there is a benefit to treating a patient suffering from tendinopathy with PRP injections.

For research in the future, a more standardized creation of the PRP injection needs to be used. To increase specificity, studies need to focus on one location in the body. These studies[3-6] looked at very different anatomical joints within the human body. While the main outcome measures examined in this critically appraised topic were patient related, imaging could be done to identify if there are physiological advantages of administering these injections to patients.

While the PRP injection is thought to alleviate symptoms of tendonitis, it is challenging to conclude that they have significant influence. All four of the studies looked at tendonitis in different regions of the body. The lack of consistency of the injection along with the lack of consistency in the tendon treated causes difficulty in synthesizing the results of this compilation to support the use of PRP injections for afflicted tendon tissues.

In conclusion, four studies[3-6] investigated the effectiveness of PRP injections on perception of pain and function in individuals with tendinitis or tendinopathy and found the PRP injections to decrease pain and increase function but there were no significant results when compared to a placebo group. Future research is needed to examine the physiological events occurring after the treatment of PRP injection to identify if the injection results in any advantage for healing of the afflicted tendon tissue. This critically appraised topic should be reviewed in two years to determine whether there is additional evidence that could change the clinical bottom line.

Resources

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2. Wroblewski AP, Mejia HA, Wright VJ. Application of platelet-rich plasma to enhance tissue repair. *Operative Technique in Orthopedics*. 2010;20(2):98-105.
3. Creaney L, Wallace A, Curtis M, Connell D. Growth factor-based therapies provide additional benefit beyond physical therapy in resistant elbow tendinopathy: a prospective, single-blind, randomised trial of autologous blood injections versus platelet-rich plasma injections. Br J Sports Med. 2011;45:966-971.
4. Kesikburun S, Tan AK, Yilmaz B, Yasar E, Yazicioglu K. Platelet-rich plasma injections in the treatment of chronic rotator cuff tendinopathy: a randomized controlled trial with 1-year follow-up. Am J Sports Med. 2013;41:2609.
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Plasma-Rich Platelet Injection Efficacy in Tendinopathy in Patients: A Critically Appraised Topic

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Introduction

Clinical Scenario: Tendinopathy is any injury to a tendon. With an injury to the tendon sheath or to the tendon, the injury response phases are activated. During the first phases of injury response, healing commences and is mediated by growth factors. Growth factors bind to cell-surface receptors and initiate an intracellular signal resulting in protein formation. The newly formed proteins regulate cell proliferation, cellular chemical movement, new blood cell formation, cell differentiation, and extracellular matrix formation; indicative of regeneration and healing. Platelets in a patient's blood are known to contain many of these desirable growth factors[1]. In a plasma-rich platelet injection, these growth factors are increased in concentration. In vitro, the plasma rich platelet (PRP) injection has been shown to promote cell proliferation, indicating the ability to halt excess inflammation while activating proliferation and maturation[2].

Focused Clinical Question: Do plasma rich platelet injections improve perceived pain and function of patients with tendinopathy in the body?

Summary of Search, "Best Evidence" appraised and Key Findings: The literature was search for studies of level 3 or higher that investigated the effects of PRP injections on pain and function in patients with diagnosed tendinopathy. Of the included articles, three studies[3,4,5] examined the effects of platelet-rich plasma injections compared to a control. One study[6] looked at the effects of one PRP injection in patients with tendinopathy over time. All studies included measures of pain as well as function.

Methods

Search Strategy
- Patient/Client group: patients with tenosynovitis
- Intervention: platelet-rich plasma injection
- Comparison: None
- Outcomes: perceived pain and function

Sources of Evidence Searched
- CINAHL
- PubMed
- Sports Discus
- MedLine

Inclusion and Exclusion Criteria

Inclusion	Exclusion
• English Language	• Case Study, Case Series, or lower than level of evidence of 2
• Published in last 10 years	• Patients without tenosynovitis
• Human beings	• Patients younger than 18 years of age
• Patients treated with PRP injection	
• Patients with tenosynovitis	

Results of Search: Four studies were located and categorized as shown in Table 1 (based on levels of evidence, Centre for Evidence Based Medicine, 2011).

Level of Evidence	Study Design	Reference
1	RCT	Creaney et al[3], Kesikburun et al[4], Krogh et al[5]
3	Cohort	Sanli et al[6]

Table 1. Summary of Study Designs of Articles Retrieved.

	Creaney et al[3]	Kesikburun et al[4]	Krogh et al[5]	Sanli et al[6]
Study Design	Randomized Control Trial	Randomized Control Trial	Randomized Control Trial	Cohort
Participants	150 participants who had failed conservative exercises for elbow tendinopathy and had symptoms for a minimum of 6 months. 87% of the participants were analyzed at follow-up date.	40 patients with a history of shoulder pain for longer than 3 months during overhead activities. 97.5% of the participants were available for final follow-up assessment.	24 patients with Achilles tendinopathy (AT) were included. The patients must have had AT symptoms for more than 6 months.	12 participants were included in this study. Had a diagnosis of distal biceps tendonitis. 100% were present for follow up.
Intervention Investigated	Patients in both groups were injected first with 2ml bupivacaine, followed by a 2-minute wait. Then patients were injected with 1.5mL blood (234 platelets X 10^9/injection) or 1.5mL PRP (652 platelets X 10^9/ injection) to the affected elbow according to grouping. All patients had two injections at time 0 and 1 month.	In all participants, injections were made under the posterolateral aspect of the acromion using real-time ultrasound guidance. First a 1% lidocaine injection was administered followed by the designated solution, 5mL PRP with a four fold increase in platelets or 5mL saline solution.	All patients underwent an ultrasound-guided injection technique. PRP and saline were injected into 7 tendon perforations in the thickest part of the tendon. 6mL of saline was injected for the control group. In the PRP injection, 6mL of PRP with a platelet concentration increased on average by 8 fold compared with whole blood.	All patients had an ultrasound-guided injection performed in a supine position. The injection of three microliters of L-PRP and sodium bicarbonate buffer was administered to the distal end of the biceps tendon.
Outcome Measures	Patient-Related tennis elbow evaluation (PRTEE) score was used to measure pain and physical function. PRTEE was completed at baseline, 1 month, 3 months, and 6 months.	The primary outcome measure was the Western Ontario Rotator Cuff (WORC) Index. The secondary outcome measures were SPADI, the Neer impingement sign, and a passive range of motion test. All were assessed at baseline, 3 weeks, 6 weeks, 12 weeks, 24 weeks, and 1 year after the injection.	The primary outcome measure was the VISA-A after 3 months. The secondary outcome measures were changes in pain at rest, when walking, and when AT was squeezed. The 3-month data was chosen as the primary data due to the extensive dropout rate.	The primary outcome measure was a VAS rest and activity pain scores. The secondary outcome measure was the EFA score. Outcome measures were assessed at baseline as well as at an average of 47 months post injection.
Main Findings	Over the course of 6 months, PRTEE scores decreased in both groups, indicative of decreased pain in both PRP injection patients as well as blood injection patients. The mean score of PRTEE was 35.8 (95% CI 30.3 to 41.4) in the PRP injection group, where the mean PRTEE score was 46.8 (95% CI 42.1 to 51.5) in the blood injection group using a X^2 test. No statistical p values were reported.	In both treatment groups, significant improvement was seen in the WORC score at all assessment points (P<.001). The SPADI and Neer impingement sign scores also showed similar improvement in both groups (P<.001). There was no statistical difference in the amount of improvement in scores between groups for any outcome measure at any time point (P>.063-.947).	There was no statistically significant difference between PRP and saline injections in the VISA-A (95% CI, P=.868). In the secondary outcome measures there were no statistically significant difference between groups. Pain at rest, P=.137, pain when walking P=.544, and pain when AT squeezed P= . 208. Tendon thickness was the only place where there was a statically significant difference, P=.030.	All patients showed significant improvement in pain and function. The VAS pre-intervention score at rest was 6 and post intervention was 0.5 with p<.002. The VAS pre-intervention score during activity was 8 and post intervention was 2.5 with p<.002. The EFA pre-intervention score was 63 and post intervention score was 90 with p<.004.
Level of Evidence	1	1	1	3
Validity Score	PEDro 10/10	PEDro 10/10	PEDro 6/10	STROBE 19/22
Conclusion	PRP and blood injections are important as a secondary option for patients with elbow tendinopathy in which conservative treatment has failed. The primary treatment of elbow tendinopathy should remain conservative treatment.	PRP injections were found to be no more effective in improving quality of life, pain, disability, and shoulder range of motion than the placebo in patients with chronic rotator cuff disease within a 1-year study. PRP injections are not supported.	1 injection of PRP when compared with one injection of saline did not result in significant improvement in perceived quality of life or decrease pain with Achilles tendinopathy.	All patients showed a significant improvement in VAS rest and activity scores and improvement in EFA scores. US-guided PRP injections were an effective treatment for symptomatic distal biceps tendinopathy.

Table 2. Characteristics of Included Studies

Clinical Bottom Line

There is inconsistent evidence to support the use of PRP injections on perception of pain and function in individuals with tendinitis or tendinopathy. Pain was not decreased due to the injection of PRP. Function did not improve faster than when compared with a saline or autologous blood injection.

Strength of Recommendation: There is a grade B evidence to support the use of PRP injection to decrease pain and increase function in patients with tendinopathy. It is a grade B of evidence because the findings of the studies[3-6] are inconsistent and do not support the use of PRP injections.

Implications for Practice, Education, and Future Research

- The four studies[3-6] included in this CAT examined the relationship between platelet-rich plasma injections and perceived pain and function in individuals suffering from tendinopathy.
- Three of the studies[3-5] revealed there was no benefit of PRP injections versus an autologous blood injection or saline injection. Sanli et al[6] concluded there was a decrease in pain and an increase in function of a person with distal biceps tendinitis following PRP injection.
- Wroblewski et al[2] stated PRP injections may halt the excess inflammation, which would inhibit the fibrous scar tissue that goes along with the healing of tendon to bone. The decreased inflammation associated with the altered healing process could suggest why three studies[3-5] showed no significant improvement compared to the control groups.
- All studies[3-6] used a outcome measures to assess patient related outcomes which include assessing pain and function through various measures. Most commonly used was the visual analog pain scale as well as different patient related outcome measures (PROM).
- A variation of concentrations of platelets was seen in all of the studies[3-5] with no report of concentration in the Sanli[6] study.
- PRP injections were not clinically proven to decrease pain or increase function any quicker than the normal healing process.
- More research in the future needs to be collected in a more athletic and younger population to be able to justify the use of the PRP injection in athletes for the treatment of tendinopathy or tendinitis. The populations used in the studies[3-6] were small and did not encompass an active group of people.
- The four studies[3-6] investigated the effectiveness of PRP injections on perception of pain and function in individuals with tendinitis or tendinopathy and found the PRP injection to be ineffective overall.

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PLATELET-RICH PLASMA INJECTION EFFICACY IN TENDINOPATHY IN ADULT PATIENTS

A Critically Appraised Topic

Hannah Johnson

CLINICAL SCENARIO

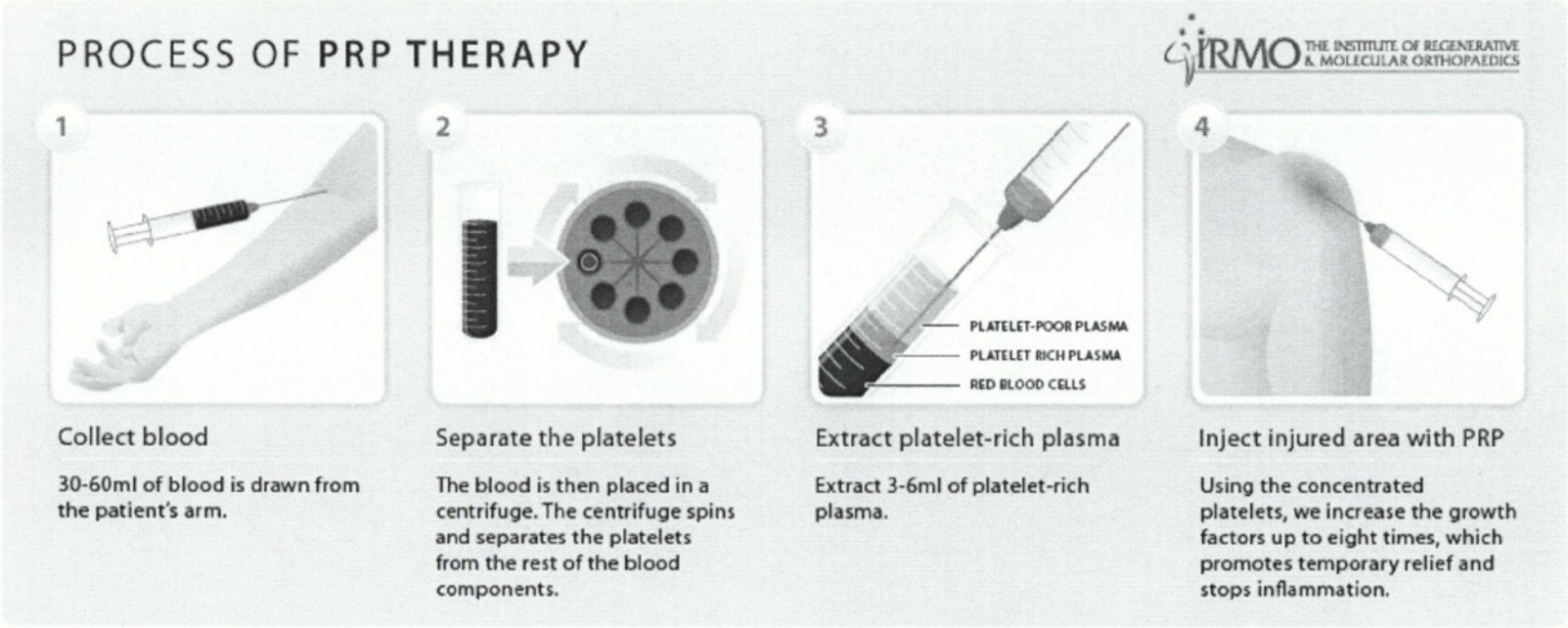

Figure 2: Process of PRP Therapy[4].

BACKGROUND- PLATELETS

- Growth Factors[1]
- Activation of growth factors leads to protein formation[2]
- Proteins regulate[1]:
  - Cell proliferation
  - Cellular chemical movement
  - New blood cell formation
  - Cell differentiation
  - Extracellular matrix formation
- Tendinitis, tennis elbow, rotator cuff repair, achilles tendon repair, muscle injuries, bone injuries, and ACL repair[1]
- Growth factors increase linearly as platelet concentration increases[1]

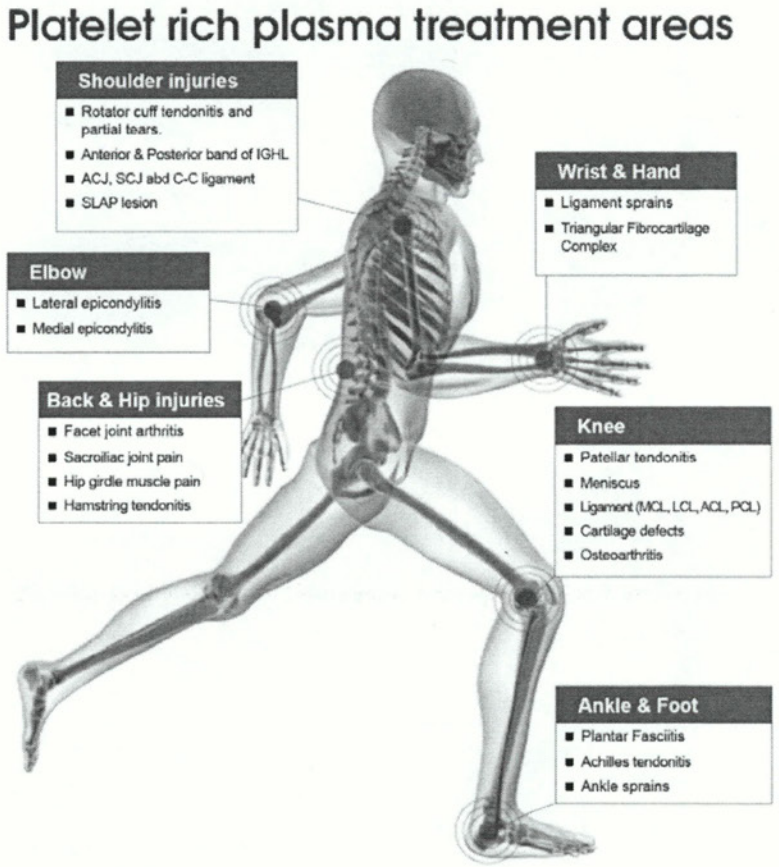

Figure 1: PRP treatment areas[3].

DO PLASMA RICH PLATELET INJECTIONS IMPROVE PERCEIVED PAIN AND FUNCTION OF ADULT PATIENTS WITH TENDINOPATHY IN THE BODY?

SOURCES OF EVIDENCE

- CINAHL
- PubMed
- Sports Discus
- MedLine

SEARCH STRATEGY/KEYWORDS

- **P**atient/Client group: patients with tenosynovitis
- **I**ntervention: platelet-rich plasma injection
- **C**omparison: None
- **O**utcomes: perceived pain and function

INCLUSION CRITERIA

- English Language
- Published in last 10 years
- Randomized Control Trial, Cohort Studies
- Participants age 18 years or older
- Human beings
- Patients treated with PRP injection
- Patients with tendinopathy

EXCLUSION CRITERIA

- Not available in English
- Published prior to 2007
- Case Study, Case Series, or lower than level of evidence of 2
- Patients without tenosynovitis
- Patients younger than 18 years of age

RESULTS OF SEARCH

Level of Evidence	Study Design	Reference
2	RCT	Creaney et al[3], Kesikburun et al[4], Krogh et al[5]
3	Cohort	Sanli et al[6]

Table 1: Summary of Study Designs of Articles Retrieved.

BEST EVIDENCE

CREANEY ET AL[5]

- Study Design: Double blind RCT
- Participants: 150 participants, 87% were analyzed for at follow up date.
- Intervention Investigated: PRP injection vs. autologous blood injection.
  - One at initial date, second at 1 month
  - 652 platelets x10 / injection
- Outcome Measure: Patient-related tennis elbow evaluation (PRTEE)
- Main Findings: Both groups scores decreased.
  - No significant difference
- Level of Evidence: 1
- Pedro 10/10
- Conclusion: PRP was not more effective in treating elbow tendinopathy than autologous blood.

KESIKBURUN ET AL[6]

- Study Design: Double blind RCT
- Participants: 40 participants with rotator cuff tendinopathy, 97.5% were analyzed for at follow up date.
- Intervention Investigated: PRP injection vs. saline injection.
  - Platelet concentration was increased by four fold
- Outcome Measure: Western Ontario Rotator Cuff (WORC), Shoulder Pain and Disability Index(SPADI), VAS with Neer Impingement test, and passive range of motion measurement
- Main Findings: Both groups scores improved.
  - No significant difference between groups
- Level of Evidence: 1
- Pedro 10/10
- Conclusion: PRP was not more effective in treating rotator cuff tendinopathy than saline injection.

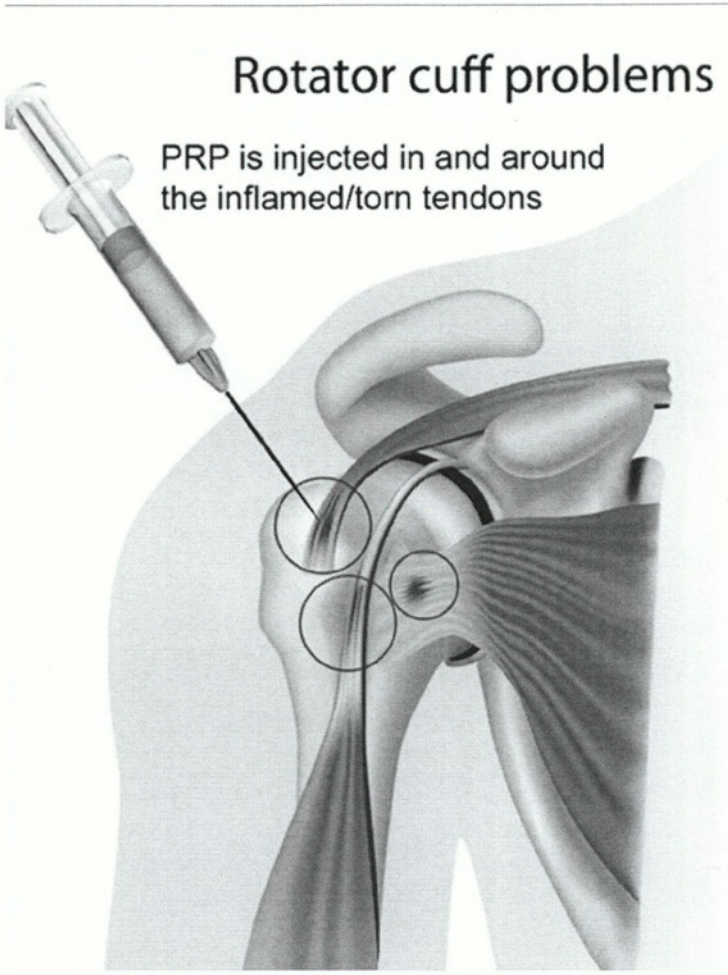

Figure 3: Rotator cuff PRP injection location[7].

KROGH ET AL[8]

- Study Design: Single blind RCT
- Participants: 24 participants, 33% were analyzed at final follow up date.
- Intervention Investigated: PRP injection vs. saline injection.
    - Platelet concentration increase by eight fold
- Outcome Measure: VISA-A (Danish patient related outcome measure), Pain Scale
- Main Findings:. No significant difference between groups
    - Tendon thickness increased after PRP injection
- Level of Evidence: 1
- Pedro 6/10
- Conclusion: PRP was not more effective in treating Achilles tendinopathy than saline injection.

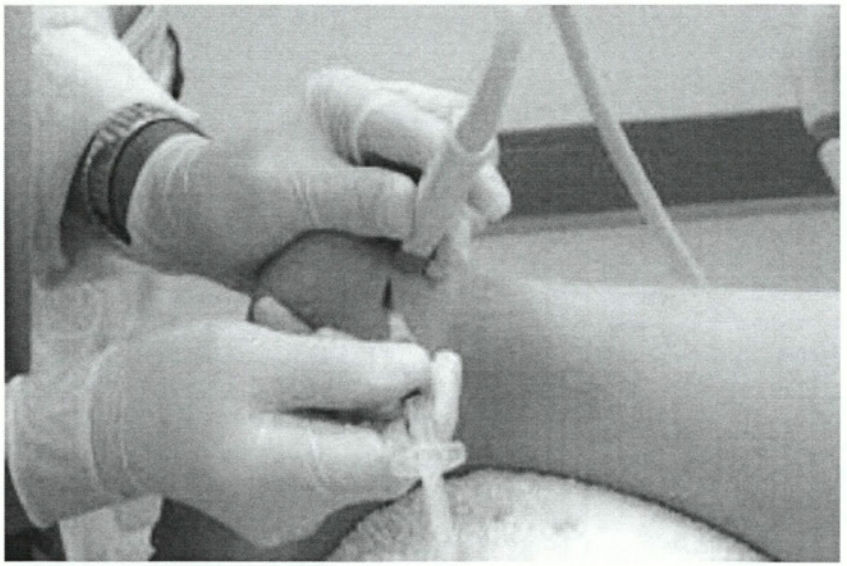

Figure 4: Ultrasound guided Achilles PRP injection[9].

SANLI ET AL[10]

- Study Design: Cohort
- Participants: 12 participants with distal biceps tendinitis, 100% were analyzed at final follow up date.
- Intervention Investigated: PRP injection
  - Platelet concentration was not reported
- Outcome Measure: Visual Analogue Scale (VAS), Elbow Functional Assessment (EFA)
- Main Findings: All patients showed significant improvement.
- Level of Evidence: 3
- STROBE 19/22
- Conclusion: PRP was effective in treating distal biceps tendinopathy.

KEY FINDINGS

- All studies were level 3 of higher
- 4 studies were included
- 3 studies looked at the effects of PRP injections versus a control
- 1 study looked at effects of PRP injections over time
- 3 studies indicated no significant differences
- 1 study indicated significant improvement

CLINICAL BOTTOM LINE

- Inconsistent evidence
- PRP injections do not effectively treat pain and function in tendinopathy patients
- Pain and function did not improve when compared to saline or autologous blood.

STRENGTH OF RECOMMENDATION

Grade B

IMPLICATIONS FOR FURTHER PRACTICE

- Normal platelet range from 150,000/μL to 350,000/μL[1]
- Platelets to 1 million per microliter, the amount of growth factor present is increased by 3 to 5-fold[2]
- 3 studies used control, 1 study looked at patient reported outcomes
- Reasons for variation
  - Differences in platelet concentration
  - Naturally occurring differences
  - Different techniques used to obtain injection
- Halt excess inflammation, while activating proliferation and maturation
- Large drop outs in Krogh[8]
- Future research
  - Population
  - Injury
  - Physiological response

CONCLUSION

Four studies[5, 6, 8, 10] investigated the effectiveness of PRP injections on perception of pain and function in individuals with tendinitis or tendinopathy and found the PRP injection to be ineffective overall.

RESOURCES

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